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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,597	10/31/2003	Leonard G. Presta	39766-0033CP2C2-C1	1656

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TH

Office Action Summary	Application No.	Applicant(s)	
	10/698,597	PRESTA ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-12* is/are pending in the application.

4a) Of the above claim(s) *10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *09/06/06;09/11/06*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

In a telephonic interview with the Attorney Jim Fox on 09/06/06, the restriction requirement of 08/24/06 was vacated, and replaced with the following restriction requirement, which was faxed to Applicant on 09/11/06..

Restriction to one of the following inventions is required under 35 U.S.C. 121:

In a telephonic conversation with the Attorney Jim Fox on 09/11/06, Applicant agreed that claims 7-12 depends on claim 6, and not claim 20, or 21. Accordingly, claims 7-12 are treated as depending on claim 6, and not on claim 20 or 21.

Claim 6 is a linking claim, linking groups 1-9. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims . Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP 804.01.

Groups 1-3. Claims 6-9, 12, drawn to a method for diagnosis of a pathological condition, which is malignancy, classified in class 435, subclass 7.1. A method detecting binding to each of the neurotrophic factors, BDNF, NT-3, and (NT-4, and NT-4/5) constitutes a single, distinct invention.

Groups 4-6. Claims 6, 10, 12, drawn to a method for diagnosis of a pathological condition, which is aberrant sprouting in epilepsy, classified in class 435, subclass 7.1. A method detecting binding to each of the neurotrophic factors, BDNF, NT-3, and (NT-4, and NT-4/5) constitutes a single, distinct invention.

Groups 7-9. Claims 6, 11-12, drawn to a method for diagnosis of a pathological condition, which is psychiatric disorder, classified in class 435, subclass 7.1. A method detecting binding to each of the neurotrophic factors, BDNF, NT-3, and (NT-4, and NT-4/5) constitutes a single, distinct invention.

The inventions are distinct, each from the other because of the following reasons.

Inventions 1-9 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The instant specification does not disclose that these methods would be used together. The method of diagnosing malignancy, aberrant sprouting in epilepsy, or psychiatric disorder are all unrelated as they have different objectives, comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Each invention performs its function using a structurally and functionally divergent material. For these reasons the Inventions 1-9 are patentably distinct.

Furthermore, the distinct steps and products require separate and distinct searches. Moreover, the searches for Groups 1-9 are not co-extensive. There may be articles devoting to a method for treating malignancy using a human trkB receptor, without discussing a method for treating aberrant sprouting in epilepsy or psychiatric disorder, or vice versa. Similarly, there may articles devoting to a method for treating malignancy, by detecting the presence of BDNF neurotrophic factor, without discussing a method for treating malignancy, by detecting the presence of neurotrophic factor NT-3 or (NT-4 or NT-4/5). As such, it would be burdensome to search the inventions of Groups 1-9 together.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the search required for each group is not required for the other groups because each group requires a different non-patent literature search due to each group comprising different products and/or method steps, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

In the reply filed on 09/21/06, Applicant's election with traverse of Group III, claims 6-9, 12, a method for diagnosis of malignancy, where the neurotrophic factor is NT-4 or NT-4/5. The traversal is on the ground(s) that the search for all claims and groups would not be an undue burden, because the pathological conditions are all treatable by the named neurotrophic factors, and since the named neurotrophic factors are often discussed in the same or related references.

This is not found persuasive because each invention performs its function using a structurally and functionally divergent material, i.e., detecting a pathological condition in different populations of patients, using different neurotrophic factors BDNF, NT-3, and NT-4 or NT-4/5, which are structurally and functionally divergent materials.

Moreover, the search for all claims and groups would cause serious burden, because the searches for Groups 1-9 are not co-extensive. Not all of the neurotrophic factors, BDNF, NT-3, and NT-4 or NT-4/5 are necessarily discussed in the same reference. For example, there may be articles devoting solely to trkB receptor and its ligand NT-4 or NT-4/5. Similarly, there may be articles devoting to a method for detecting malignancy using a human trkB receptor, without discussing a method for detecting aberrant sprouting in epilepsy or psychiatric disorder, or vice versa. The requirement is still deemed proper and is therefore made FINAL.

Accordingly, group III, claims 6-9, 12, a method for diagnosing malignancy or tumor, by detecting the human trkB receptor bound to NT-4 or NT-4/5, are examined in the instant application.

Information Disclosure Statement

The information disclosure statement of 10/31/03, including the submitted PTO-1449, could not be considered, because it belongs to the parent case, SN 09/724, 524, and not to the instant application SN 10/698,597.

Priority Date

It is noted that a review of the parent applications SN 09/724524 filed on 11/27/2000, 09/156923 filed on 09/18/1998, 08/359,705 filed on 12/20/1994, 08/286,846 filed 08/05/1994, and 08/215,139 filed 03/18/1994 does not reveal any support for claims 6-9, 12 . Therefore the Examiner is establishing a priority date for claims 6-9, 12 as the filing date of the instant application, 10/31/2003.

If Applicant disagrees with any rejection based on the Examiner's establishment of a priority date (give date) for the instantly claimed application serial number 10/698597, applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

Oath or Declaration

This application seems to be a continuation-in-part and not a divisional of the parent applications for the following reasons.

This application presents a claim for subject matter not originally claimed or embraced in the statement of the invention, in view that a review of the parent applications SN 09/724524 filed on 11/27/2000, 09/156923 filed on 09/18/1998, and 08/359,705 filed on 12/20/1994 does

not reveal any support for claims 6-9, 12, although the instant application claims to be a divisional of the parent application SN 09/724524 filed on 11/27/2000, 09/156923 filed on 09/18/1998, and 08/359,705 filed on 12/20/1994.

A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP § § 602.01 and 602.02.

Objection

Claims 7-9, 12 are objected to, because they depend on non-elected claims 20-21, which do not exist. This objection could be obviated, by amending the claims for example to recite "the method of claim 6".

For the purpose of compact prosecution, and in view of the telephonic conversation with the Attorney Jim Fox on 09/11/06, claims 7-9, 12 are treated as depending on claim 6.

Specification

1. Figure 1 legend on page 11 is objected to, because it is not clear the amino acid sequence and the nucleotide sequence of the truncated form of human trkB receptor are attached to what.

2. The amendment of the specification submitted on 10/31/03 is not entered for the following reasons: In the amended figure 4 legend, it is not clear what are the closed triangle in TrkA, the half closed triangle in trkC, and the smaller and larger open triangles in trkC.

3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Proper correction of the specification to incorporate the subject matter recited in the new claims 6-9, 12 is required.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-9, 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the limitation "said neurotrophic factor". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-9, 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses that the term trk receptor, with or without an affixed capital letter (B), includes full length receptors, their truncated and variant forms, such as those arised by alternative splicing and/or insertion, and naturally-occuring allelic variants, and well as functional derivatives of such receptors (p.16, lines 22-31). The specification also discloses that the term neurotrophin or neurotrophic factor and their grammatical variants are used interchangeably (p.15, last paragraph).

In view of the disclosure in the specification, the term "trkB receptor" as cited in claim 6, without being accompanied by a sequence identification number, reasonably reads on a genus of variants trkB receptors, with unknown structure. Similarly, the term "NT-4 or NT-4/5" without being accompanied by a sequence identification number, reasonably reads on a genus of variant neurotrophic factors NT-4 or NT-4/5.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not

> define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that □the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not

adequately describe a product itself logically cannot adequately describe a method of using that product.

In this case, the specification does not describe the human trkB receptor, and the neurotrophic factor NT-4, or NT-4/5 in a manner that satisfies either the standards as shown in the example of Lilly or Enzo. The specification does not provide sufficient structure or common structure, other than the single human trkB receptor SEQ ID NO:2, and its single spliced variant, the truncated intracellular domain, SEQ ID NO:40 (see figure 1 legend on page 3), to support the broad breath of the claimed genus. Nor is there any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single human trkB receptor, SEQ ID NO:2, and its spliced variant SEQ ID NO:40, this does not provide a description of the the human trkB receptor, and the neurotrophic factor NT-4, or NT-4/5 that would satisfy the standard as shown in the example of Enzo.

The specification also fails to describe the human trkB receptor, and the neurotrophic factor NT-4, or NT-4/5, by the standards shown in the example in Lilly. The specification describes only a single human trkB receptor, SEQ ID NO:2, and its spliced variant SEQ ID NO:40. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The specification does not provide an adequate written description of the human trkB receptor, and the neurotrophic factor NT-4, or NT-4/5 that is required to practice the claimed invention. Thus, the specification does not meet the 112, first paragraph written description requirement, and one of skill in the art would reasonably conclude that Applicant did not have

possession of the claimed human trkB receptor, and neurotrophic factor NT-4, or NT-4/5 at the time the invention was made. Since the specification fails to adequately describe the product for use in the claimed method, it also fails to adequately describe the claimed method.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 6-9, 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is noted that neurotrophin is the same as neurotrophic factor. It is further noted that a tumor encompasses any enlargement or abnormal growth, which is not necessarily cancerous, for example, cystic of the pancreas, splenic tumor or enlargement of the spleen, etc...
(Stedman's medical dictionary, 25th ed, 1990, p.1652-1653).

The following *Wands* factors have been considered when the 112, first paragraph, enablement rejection was made:

The breadth of the claims

The breadth of the claims is broad. The claims 6-9, 12 reasonably read on a method for diagnosis of **any** pathological conditions, **any** malignancies, **any** abnormal growths, or **any** pancreatic disorders, characterized by the endogenous production of a neurotrophin capable of binding to a human trkB receptor, using as a probe a **variant** human trkB receptor to detect its binding to its ligand, a **variant** NT-4 or NT-4/5 neurotrophin.

The nature of the invention

The nature of the invention is complex, encompassing a method for diagnosis of **any** pathological conditions, any malignancies, any tumors or abnormal growths, or any pancreatic disorders, characterized by the endogenous production of a neurotrophin that is a ligand for a human trkB receptor, using as a probe a **variant** human trkB receptor to detect its binding to its ligand, a **variant** NT-4 or NT-4/5 neurotrophin.

The state of the prior art

The prior art teaches underexpression of NT-4 in pancreatic cancer, as compared to normal pancreatic tissue (see 103 below). The prior art does not teach a method for detecting any pathological conditions, any cancers, any abnormal growths, or any hepatic disorders, by detecting the presence of NT-4 or NT-4/5, using a human trkB receptor.

The level of one of skill in the art

Although the level of skill in the field of molecular pathology is high, it would be undue experimentation for one of skill in the art to practice the claimed invention.

The level of predictability of the art

The level of unpredictability in the art is high.

One cannot predict which of the claimed numerous pathological conditions, cancers, abnormal growths, or pancreatic disorders actually produce the neurotrophin NT-4 or NT-4/5, which neurotrophin NT-4 or NT-4/5 does not exist in the corresponding control sample, because

of the following reasons: Expression of a new protein in a pathological condition, cancer, abnormal growth, or pancreatic disorder is not a predictable event. For example, Soontornniyomkij et al, 1999 (Acta neuropathologica 98(4): 345-8) teach that expression of trkB proteins is characteristic of particular disease processes, as shown by the absence of BDNF and trkB protein in glia cells in AD patients, in contrast to their presence in HIV patients (abstract, last seven lines). Similarly, Guate et al, 1999 (BJU Internatl, 84: 495-502) teach that trkA and TrkC are overexpressed in prostate cancer, as compared to normal prostate tissue, while trkB is not detected in prostate cancer (abstract, p.496, second column, last paragraph).

Moreover, the structure and function of the encompassed variant human trkB receptors, and variant neurotrophins NT-4 or NT-4/5 cannot be predicted, in view of the unpredictability of protein chemistry. For example, one cannot predict whether a variant human trkB receptor still maintains its binding property to the ligand NT-4 or NT-4/5, or variant thereof, because the ligand and the receptor have to have a certain molecular configuration specificity, for example, a certain configuration for binding of the ligand into the receptor. Bowie (Science, 1990, 257:1306-1310) teaches that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie further teaches that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of

maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein.

Working example and The amount of direction provided by the inventor

The specification only discloses detection of the full length 8.1 kb transcript of trkB, and at least one truncated 6.9 kb transcript of trkB in normal healthy human. The 8.1 kb trkB mRNA is in greater abundance in the human brain, besides its presence in kidney, skeletal muscle and pancreas, and of the truncated form is in heart, spleen and ovary (page 104, figure 6 and figure 6 legend on pages 12-13).

There is no disclosure in the specification which pathological conditions, which cancers, which tumors, or which pancreatic disorders express the neurotrophin NT-4 or NT-4/5, or variant thereof, wherein said neurotrophin does not exist in the corresponding control sample, and

wherein said neurotrophin could be detected by the human trkB receptor protein or a variant thereof.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, it would have been undue experimentation for one of skill in the art to practice the claimed invention.

Moreover, claims 6-9, 12 are also rejected under 112, first paragraph, because the cited NT-4 and NT-4/5 are essential materials for the claimed method, which are however only incorporated by reference to publications in the art (see the instant specification, page 2, last paragraph, bridging page 3). MPEP 608.01 teaches that incorporation of **essential material** in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference

(see 37 CRF 1.57). The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973) (see MPEP 6.19 and 6.19.01) . In other words, Applicant is required to submit a paper copy and a computer readable form copy of the NT-4 or NT-4/5 sequence cited in the published reference as referred to in the specification, and a statement that the content of the paper and computer readable copies are the same, and include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). Applicant is also required to submit an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application.

Conclusions

No claims are allowed.

The closiest prior art is Schneider M B et al, 2001 (J Histochem & Cytochemistry, 49 (10): 1205-1210). Schneider et al teach detection of NT-4, which is expressed in cancerous pancreatic tissue, and not in normal pancreatic tissue, using an anti-NT-4 antibody. However, Schneider et al do not teach detection of NT-4 using a human trkB receptor.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
October 11, 2006

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER